

Malignant Paraganglioma of the Thyroid Gland: A Case Study

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Background Information:

Paraganglia are neural crest derived cells, and as such, they are found along the embryologic migration routes of neural crest tissue from the base of the skull to the lower pelvis, not including the area of the extremities.^{1,2} They are most closely associated with blood vessels, where they act as chemoreceptors, such as in the carotid body.¹ Paragangliomas are neoplasms that arise from these paraganglia, usually as a benign tumor. These extra adrenal paragangliomas are histochemically non-chromaffin, and tend to be located in the head and neck region, superior mediastium, and retroperitoneum.³ Specifically, the most common locations are the carotid body, jugular bulb, Jacobson's tympanic plexus in the middle ear, and the vagal nerve.² Overall, paraganglioma of the head and neck region are incredibly rare and constitute only 0.012% of tumors in that area, and due to their strong association with blood vessels, an overwhelming 80% of these paragangliomas arise from the carotid body.^{1,3}

Thyroid associated paraganglioma is especially uncommon as it is not an area that should contain neural derived tissue. There are only 28 recorded cases of primary thyroid paraganglioma in the English-based publication, and their origin is still not fully understood.² Although it is not known for sure how it forms, it is thought that the paraganglioma arises from the inferior laryngeal paraganglia, which are being displaced downwards to the lateral aspects of the thyroid gland, or that the paraganglioma is formed in the thyroid capsule itself.^{2,4}

Case History:

The patient was a 68 year old female with a history of a solitary thyroid nodule in the right lobe. She was diagnosed with hypertension and sarcoidosis previously, but was currently in remission. There were no changes in her voice or dysphagia, and she was biochemically euthyroid. CT scans showed low grade uptake in an enlarged right thyroid lobe with mass effect on the hypopharyngeal airway with mild posterior and substernal extension in the mediastinum. The scan also showed two involved cervical lymph nodes, a level II on the left and a level V on the right. Multiple attempts at fine needle aspiration biopsy were not successful.

She underwent a total thyroidectomy to remove the thyroid and impacted nodes. The thyroid mass was firm and immobile, and showed significant vascularity that posed tremendous issues with bleeding. The right lobe was also adherent to the right cricothyroid muscles. Upon closer inspection, there was a significant amount of tumor around the nerve and invading into the right, first tracheal ring, as well as the cricothyroid cartilage and muscle. Frozen sections on the excised tissue provided a diagnosis of possible medullary thyroid carcinoma.

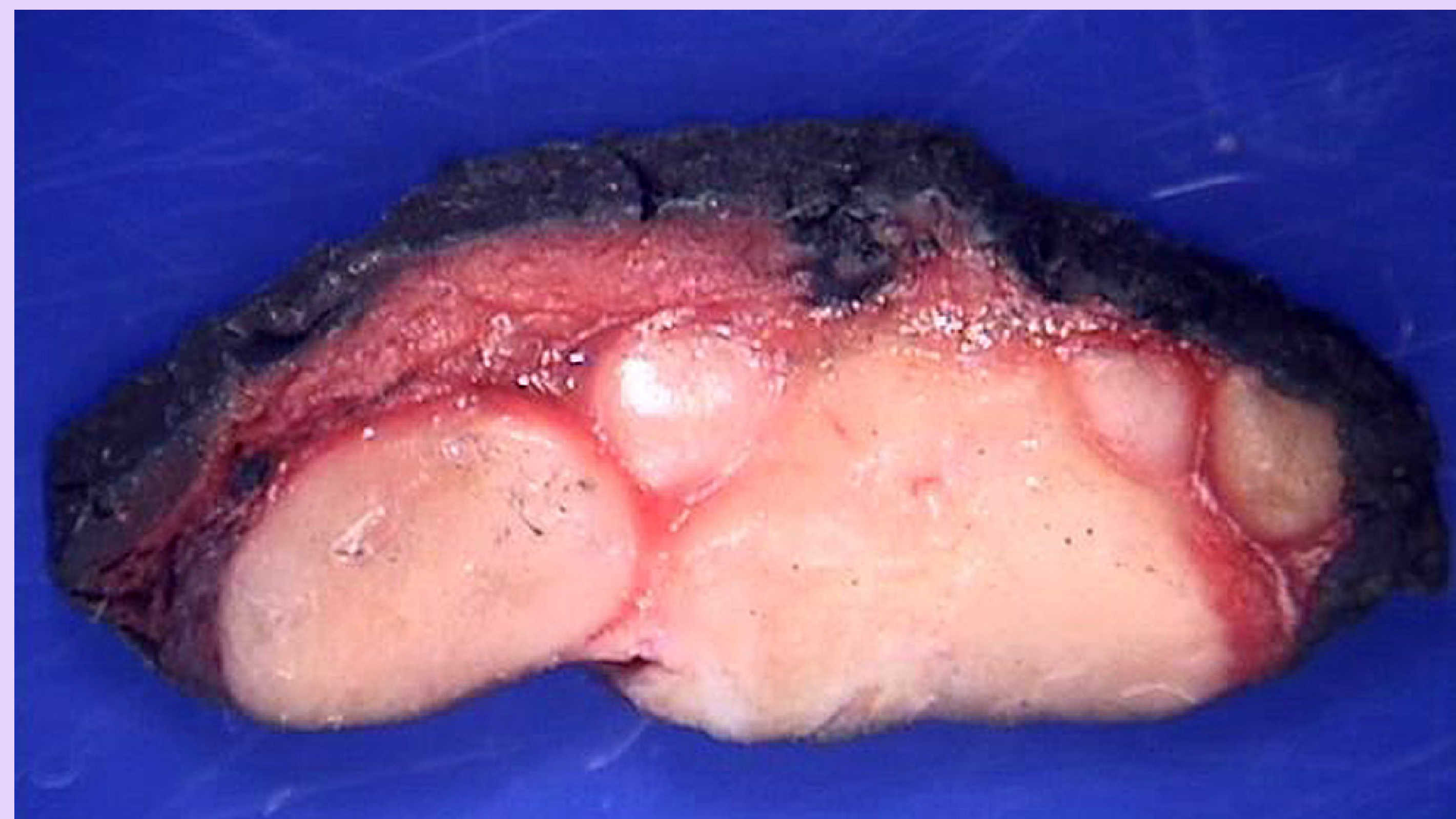


Figure 1. Gross photograph of paraganglioma mass involving almost the entire right lobe.

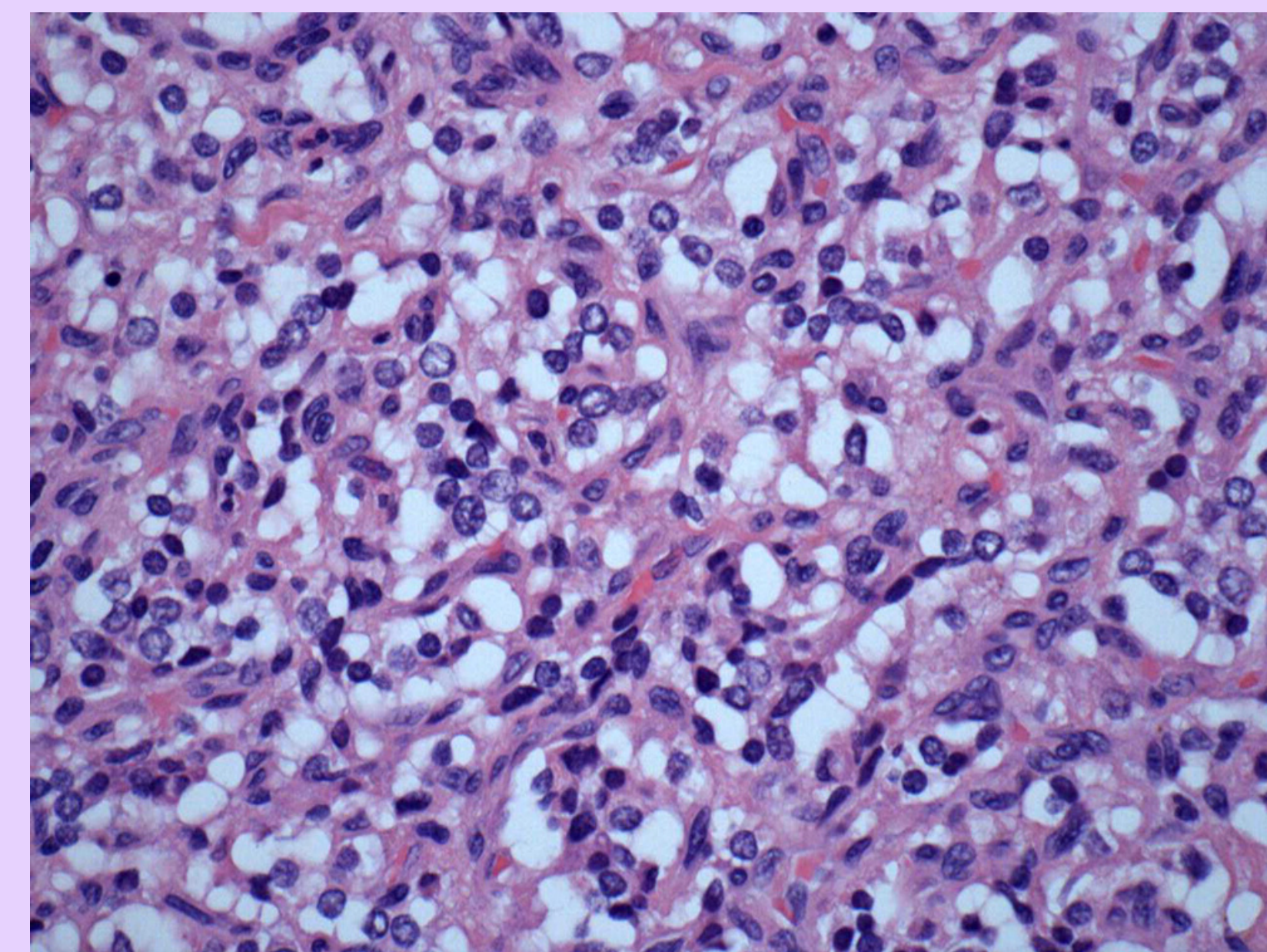


Figure 2. H&E stain demonstrating the classic zellballen (nesting) pattern (40x).

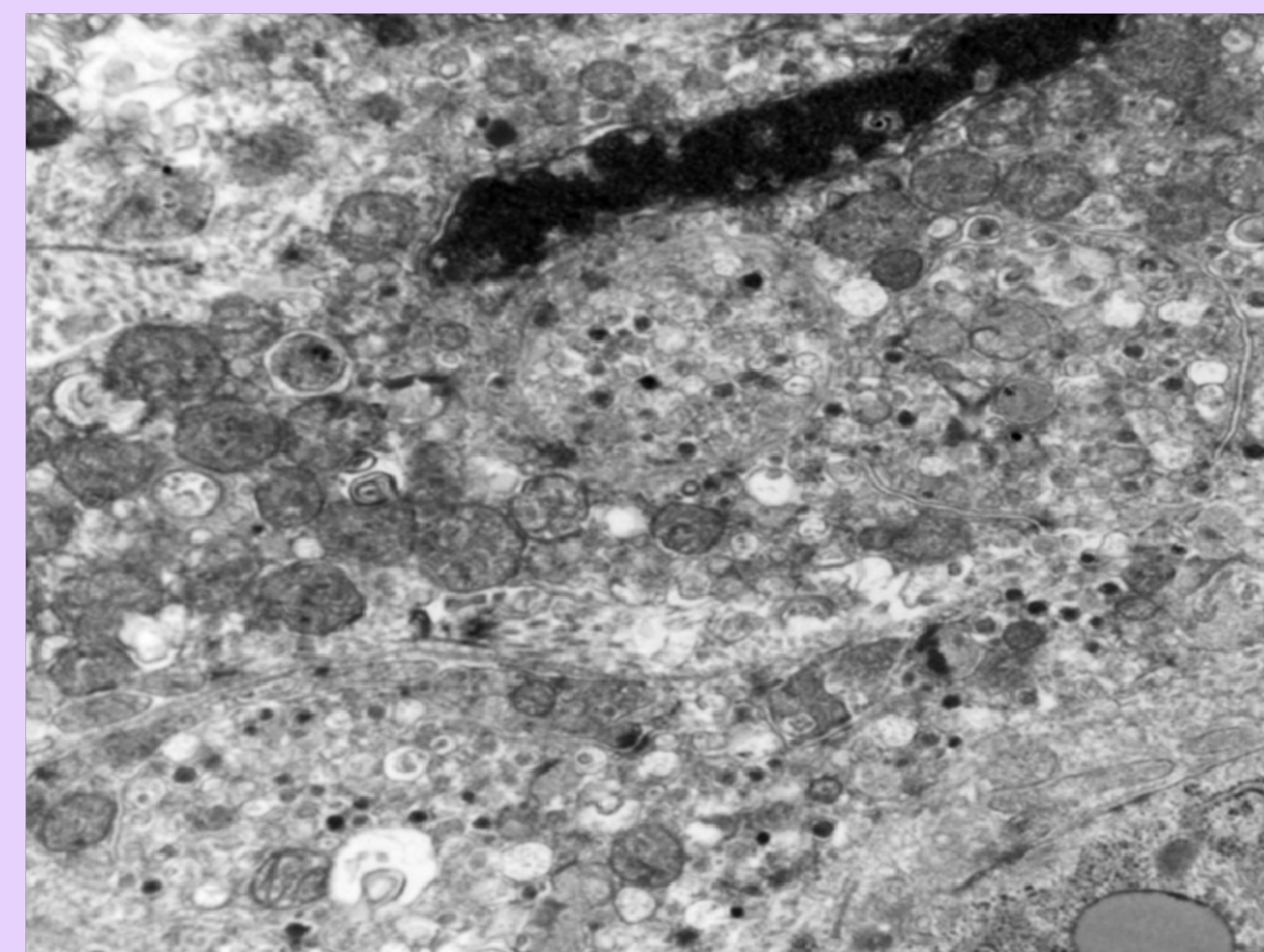


Figure 3. EM showing dense core neurosecretory granules of the chief cells.

Methods:

Gross dissection revealed a 2.2 x 1.5 x 1.2cm mass involving almost all of the right lobe. Light microscopy with Hematoxylin and Eosin (H&E) staining distinctly showed that it was composed of a thin, fibrous capsule with multiple satellite nodules away from the main mass. There were large lobules surrounded by fibrovascular bands, and within the lobules the tumor (chief) cells and sustentacular support cells were distributed with a focal zellballen (nesting) pattern. This is the standard appearance for paraganglioma and helps to eliminate the differential diagnosis of gross look alike hyalinizing trabecular adenoma, although it does not remove the differential option of medullary carcinoma of the thyroid.

Immunohistochemistry (IHC) stains showed that the tumor cells expressed neuro-specific enolase (NSE), chromogranin A, synaptophysin, vimentin, and CD56, and the sustentacular support cells around the chief cells were positive for expression of S-100. All of these stain responses are common positive reactions for paraganglioma. IHC stains were also negative for calcitonin, thyroglobulin, TTF-1, and multiple cytokeratins. These stains are usually positive in primary thyroid carcinomas, such as the other major look alike, medullary carcinoma of the thyroid. EM showed that the chief cells contained varying amounts of cytoplasmic dense-core granules with spindle-shaped sustentacular cells located peripherally. These neoplastic cells were also located in the left lobe of the thyroid, the right cricoid, and the soft tissue from around the thyroid.

The left paratracheal node showed 0.2cm of neoplastic cells, which were confirmed as metastatic with a positive synaptophysin, chromogranin A, and NSE IHC stain.

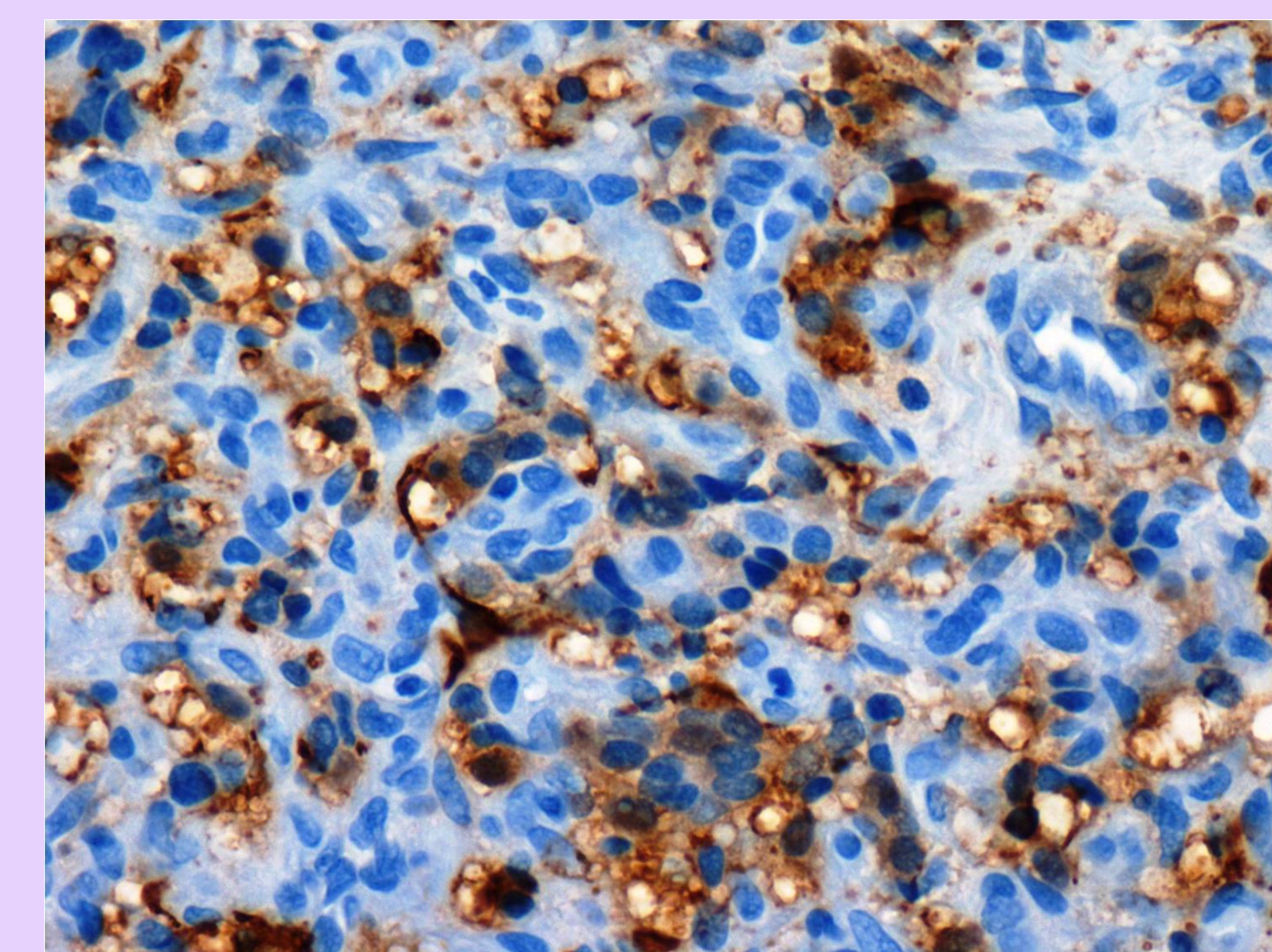


Figure 4. Sustentacular cells staining positive for S-100 protein (40x).

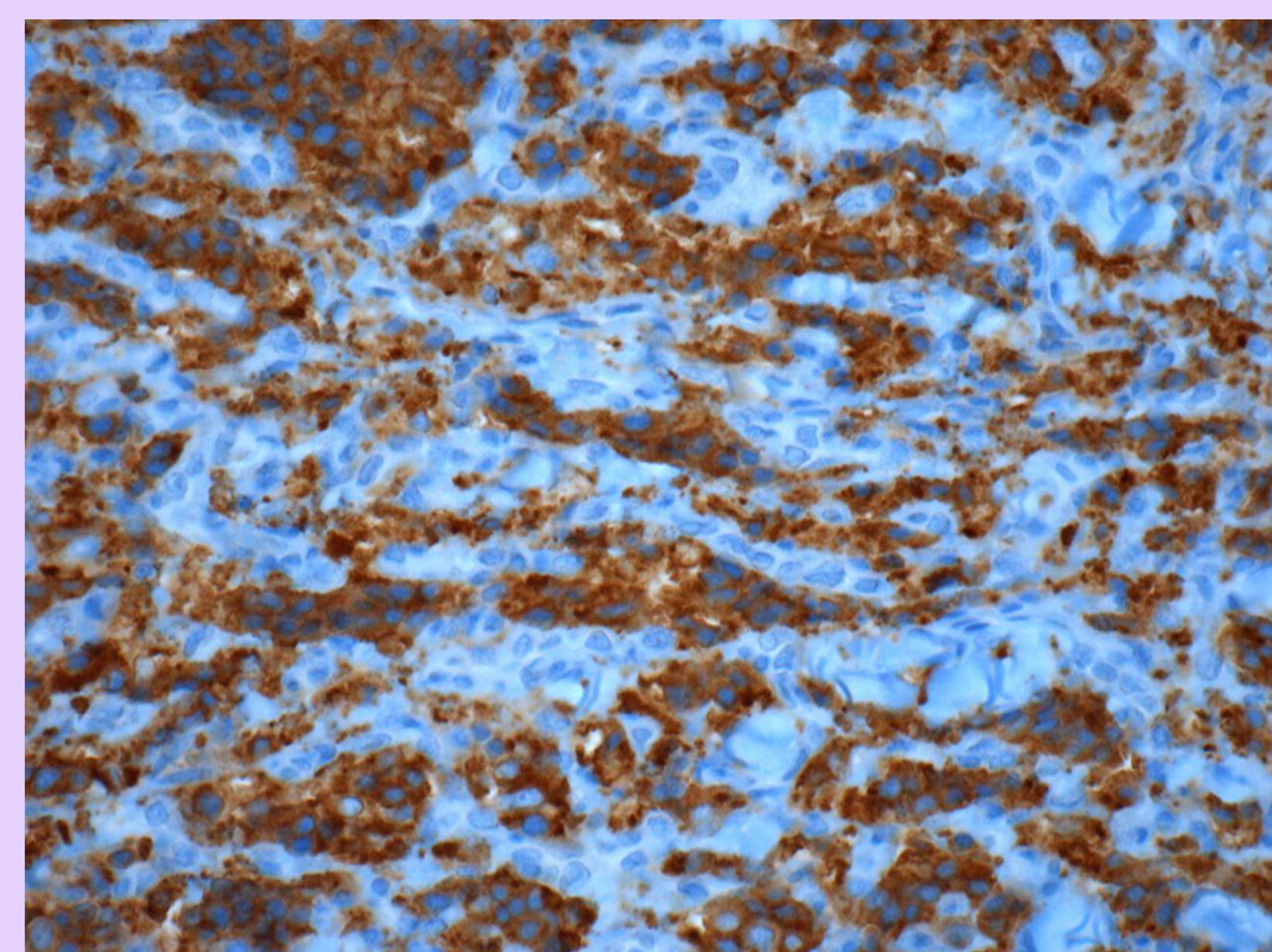


Figure 5. Tumor (chief) cells staining positive for synaptophysin (40x).

Results:

Final diagnosis was a malignant paraganglioma of the thyroid due to the presence of metastasis to the paratracheal lymph node. There was also extrathyroidal extension, although this could be due to the size of the tumor. Patient then underwent adjuvant radiation therapy and was directed to follow up for adjunct PET/CT scans to see if any additional systemic therapy is necessary.

Conclusion:

Distinction should also be made between benign and malignant paragangliomas of the thyroid, although malignant types are incredibly rare. Pathologists are not able to use IHC and H&E to distinguish between benign and malignant. Therefore the only way to diagnose a paraganglioma of the thyroid as malignant is if it metastasizes to non-neuroendocrine tissue, usually the cervical lymph nodes.² Origin for the paraganglioma is also very important, as they can be familial or sporadic. Sporadic makes up the majority of cases at about 90%, but familial is not to be overlooked. In those who have familial paragangliomas, and in 10% of sporadic paragangliomas, there is a 30% risk of mutations in the genes encoding for mitochondrial complex II (SDHB, SDHC, SDHD). Individuals with this are at risk of multiple tumors.^{1,2} Because of these potential mutations, or in the case of malignant paraganglioma, follow up is crucial in treatment.

Because they are so rare, paraganglioma is not commonly listed in differential diagnoses for thyroid gland lesions. Usually they are discovered through signs and symptoms, mass effect indications, as an incidental finding on a imaging scan of the thyroid, or during a familial screen for hereditary paraganglioma.⁵ Often when the growth is discovered it is initially misdiagnosed as a more common thyroid nodule, which occur in 5% of women and 1% of men, making it far more likely than paraganglioma.¹ Despite this fact, modern imaging and staining has given a reliable set of guidelines to help distinguish between paraganglioma and its more frequent thyroid malignancy lookalikes, most commonly hyalinizing trabecular adenoma of the thyroid and medullary carcinoma of the thyroid.

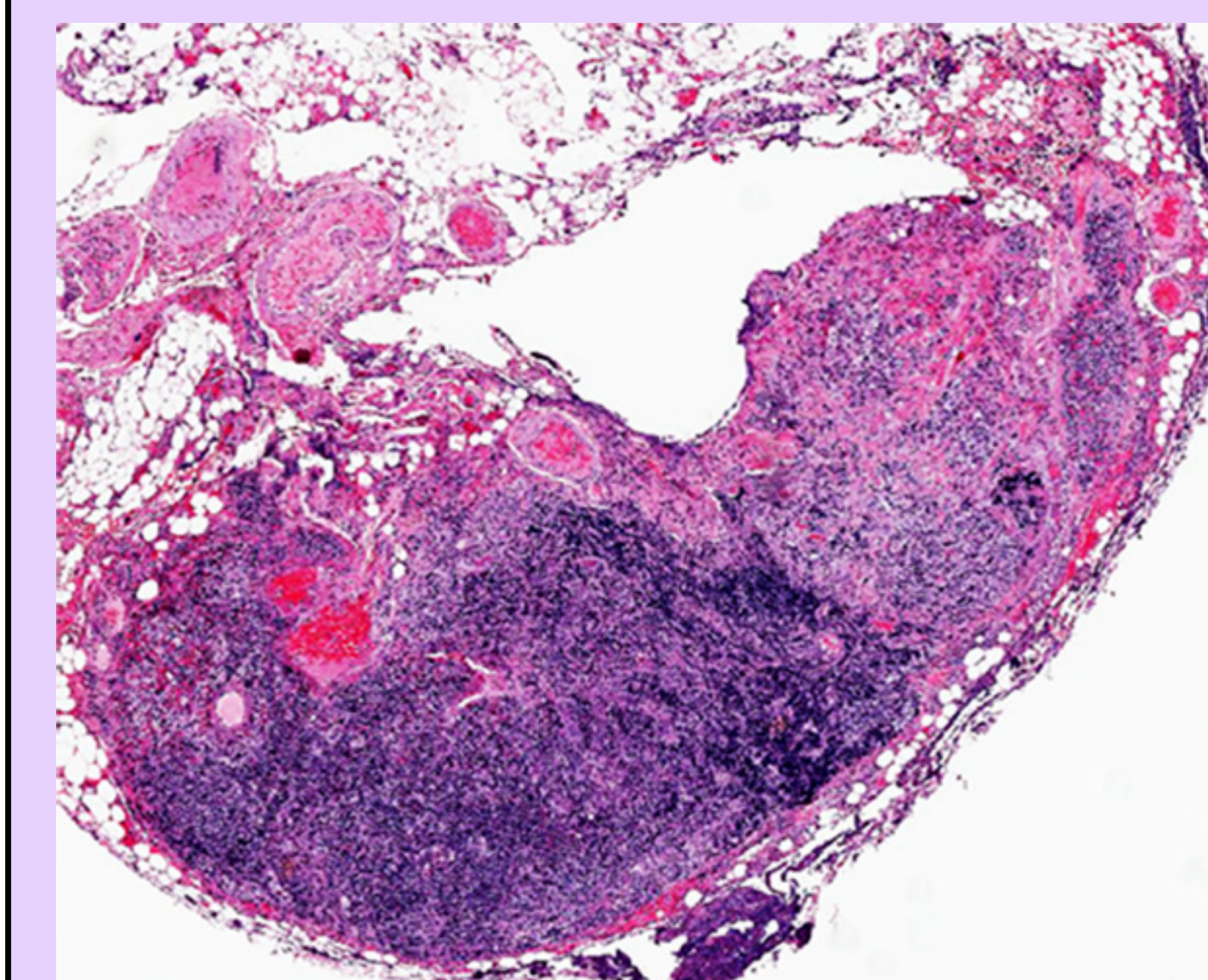


Figure 6. H&E stain showing 0.2cm of metastatic tumor cells in the lymph node (40x).

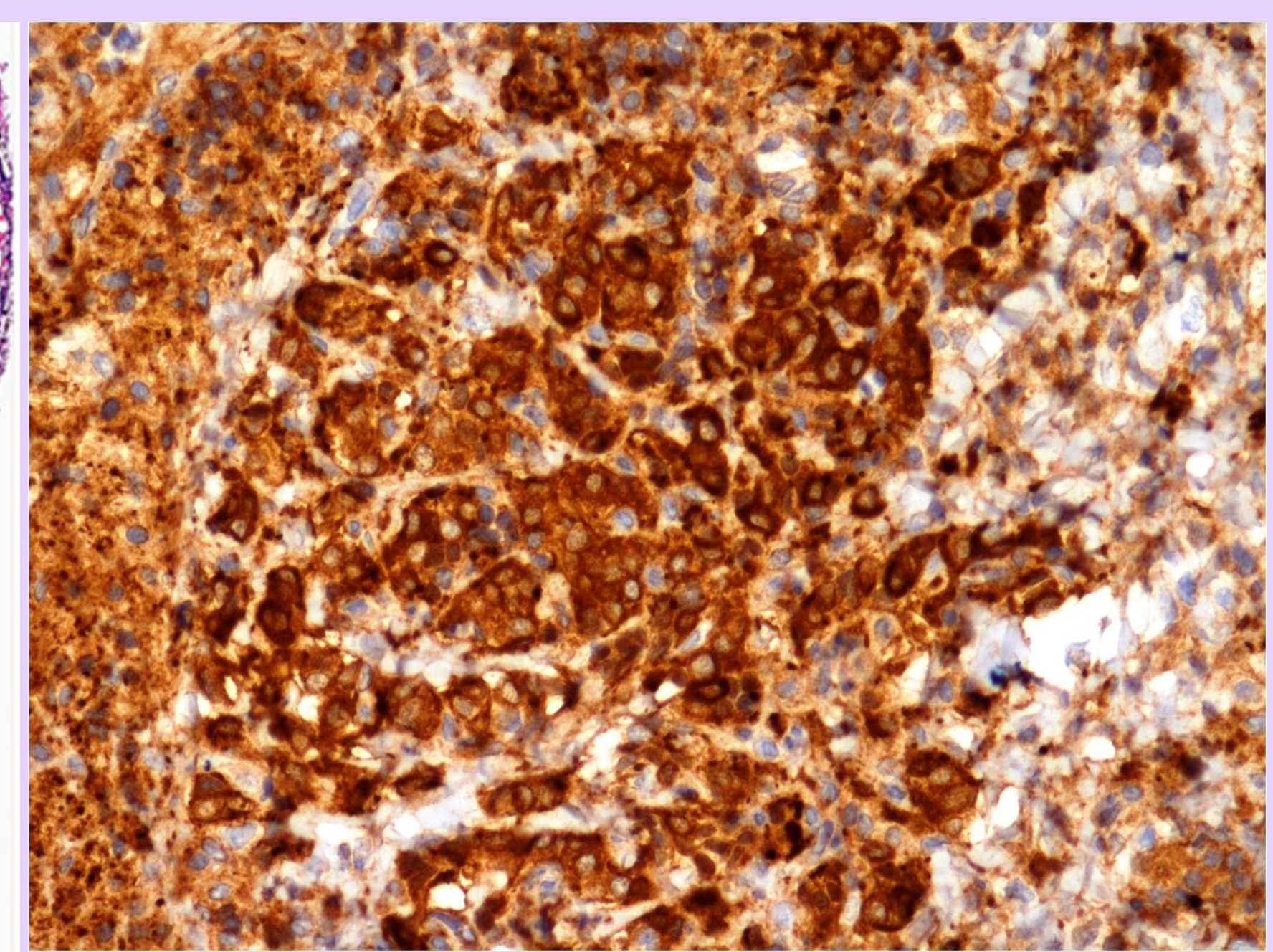


Figure 7. Positive NSE stain confirming metastatic tumor cells in the lymph node (40x).

References:

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